Docket No.: 086016-0034 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Tara BIELSKI, et al.

Application No.: 10/800,031

Customer No.: 20277

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Confirmation No.: 6868

Group Art Unit: 1615

Examiner: Bethany BARHAM

Title: NOVEL ORALLY ADMINISTRABLE FORMULATION OF NITROFURANTOIN AND A METHOD FOR PREPARING SAID FORMULATION

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Appeal Brief is submitted in support of the Notice of Appeal filed May 9, 2011, and is accompanied by a petition for a three month extension of time.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

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Real party in interest

The real party in interest is Mylan Pharmaceuticals, Inc. by way of an assignment recorded on June 23, 2004 at Reel 014862, Frame 0995.

Related appeals and interferences

None

Status of the claims

1. Claims withdrawn from consideration, but not canceled: 61-65.

3. Claims pending: 1-60 and 66.

4. Claims rejected: 1-60 and 66.

5. Claims on appeal: 1-60 and 66.

Status of the amendments

No Amendment was filed following the November 9, 2010 final Office Action.

Summary of the claimed subject matter

Each of the pending claims is an originally filed claim.

The subject matter of independent claim 1 relates to an orally administrable formulation for administering nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) the first component comprises nitrofurantoin monohydrate, sodium alginate, alginic acid and hypromellose; (b) the second component comprises macrocrystalline nitrofurantoin; and (c) the formulation provides a therapeutically effective combination of the nitrofurantoin monohydrate and the macrocrystalline nitrofurantoin.

The claim phrase "an orally administrable formulation for administering nitrofurantoin to a patient in need thereof" is supported in the specification at, for example, the abstract and paragraphs 10 and 15. The claim phrase "a first component being a controlled release form" is supported in the specification at, for example, the abstract, and paragraphs 10 and 16. The claim phrase "a second component being an immediate release form" is supported in the specification at, for example, the abstract, and paragraphs 10 and 16. The claim phrase "wherein (a) said first component comprises nitrofurantoin monohydrate, sodium alginate, alginic acid and hypromellose" is supported in the specification at, for example, the abstract and paragraphs 11 and 17-21. The claim phrase "(b) said second component comprises macrocrystalline nitrofurantoin" is supported in the specification at, for example, the abstract and paragraphs 12, 24, and 25. The claim phrase "(c) said formulation provides a therapeutically effective combination of said nitrofurantoin monohydrate and said macrocrystalline nitrofurantoin" is supported in the specification at, for example, paragraphs 9, 13, 45, and 87.

The subject matter of independent claim 30 relates to an orally administrable formulation for the administration of nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) the first component comprises: nitrofurantoin monohydrate in an amount of from about 5% to about 50% by weight of the first component; hypromellose in an amount of from about 5% to about 90% by weight of the first component; sodium alginate in an amount of from about 2% to about 80% by weight of the first component; alginic acid in an amount of from about 2% to about 80% by weight of the first component; a diluent in an amount of from about 2% to about 90% by weight of said first component; and a lubricant in an amount of from about 0.1% to about 6% by weight of the first component; and (b) the second component comprises: macrocrystalline nitrofurantoin in an amount of from about 3% to about 35% by weight of the second component; a diluent in an amount of from about 5% to about 90% by weight of the second component; and a lubricant in an amount of from about 0.1% to about 6% by weight of the second component; and the first and second components are present in a wt:wt ratio of from about 1:1 to about 5:1.

Support for the amount of nitrofurantoin monohydrate can be found in the specification at paragraph 18. Support for the amount of hypromellose can be found in the specification at paragraph 19. Support for the amount of sodium alginate can be found in the specification at paragraph 20. Support for the amount of alginic acid can be found in the specification at paragraph 21. Support for the amount of a diluent in the first component can be found in the specification at paragraphs 22 and 74. Support for the amount of lubricant in the first component can be found in the specification at paragraphs 23 and 73. Support for the amount of macrocrystalline nitrofurantoin can be found in the specification at paragraphs 25 and 60.

Support for the amount of diluent and lubricant in the second component can be found in the specification at paragraphs 26 and 74, and 27 and 73, respectively. Support for the wt:wt ratio of the first and second components can be found in the specification at paragraphs 28 and 54.

The subject matter of independent claim 37 relates to an orally administrable formulation for the administration of nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) the first component comprises: nitrofurantoin monohydrate in an amount of about 20% by weight of the first component; hypromellose in an amount of about 20% by weight of the first component; sodium alginate in an amount of about 20% by weight of the first component; and alginic acid in an amount of about 20% by weight of the first component; microcrystalline cellulose in an amount of about 9% by weight of the first component; dibasic calcium phosphate in an amount of about 10% by weight of the first component; and magnesium stearate in an amount of about 1% by weight of the first component; and (b) the second component comprises: macrocrystalline nitrofurantoin in an amount of about 12.5% by weight of the second component; lactose in an amount of about 43% by weight of the second component; microcrystalline cellulose in an amount of about 43% by weight of the second component; and magnesium stearate with sodium lauryl sulfate in an amount of about 1% by weight of the second component; and the first and second components are present in a wt:wt ratio of from about 1:1 to about 5:1.

Support for the amount of nitrofurantoin monohydrate can be found in the specification at paragraph 32. Support for the amount of hypromellose can be found in the specification at paragraph 33. Support for the amount of sodium alginate can be found in the specification at paragraph 34. Support for the amount of alginic acid can be found in the specification at

paragraph 35. Support for the amount of microcrystalline cellulose can be found in the specification at paragraph 36. Support for the amount of dibasic calcium phosphate can be found in the specification at paragraph 37. Support for the amount of magnesium stearate can be found in the specification at paragraph 38. Support for the amount of macrocrystalline nitrofurantoin can be found in the specification at paragraph 40. Support for the amount of lactose in the second component can be found in the specification at paragraph 41. Support for the amount of microcrystalline cellulose in the second component can be found in the specification at paragraph 42. Support for the amount of magnesium stearate with sodium lauryl sulfate in the second component can be found in the specification at paragraph 43. Support for the wt:wt ratio of the first and second components can be found in the specification at paragraph 54.

The subject matter of independent claim 50 relates to a method for preparing a formulation which comprises (a) admixing nitrofurantoin monohydrate, hypromellose, alginic acid sodium alginate and at least one pharmaceutically acceptable carrier and forming the admixture into a controlled release first component; and (b) admixing macrocrystalline nitrofurantoin and at least one pharmaceutically acceptable carrier and forming the admixture to form an immediate release second component.

Support for the method of claim 50 can be found in the specification at paragraphs 79-81.

Grounds of rejection to be reviewed on appeal

Whether claims 1-60 and 66 are obvious under 35 U.S.C. § 103(a) over U.S. Patent No. 4,772,473 in view of U.S. Patent Publication No. 2003/0180359 or U.S. Patent No. 4,792,452 and U.S. Patent No. 5,415,871.

Arguments

The rejection under 35 U.S.C. § 103(a)

Claims 1-60 and 66 have been rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,772,473 ("the '473 patent") in view of U.S. Patent Publication No. 2003/0180359 ("the '359 publication") or U.S. Patent No. 4,792,452 ("the '452 patent") and U.S. Patent No. 5,415,871 ("the '871 patent").

The Examiner's Position:

According to the Examiner, the '473 patent discloses all of the limitations of the instant claims except for the controlled release excipients (Office Action dated Nov. 9, 2010, p. 3), a tablet, and the specific percentages (*Id.* at 4). The Examiner states that the '359 publication discloses multi-layer dosage forms such as caplets and tablets; and controlled release polymers/excipients such as PVP, HPMC, carboxyvinylpolymers, alginic acid and derivatives such as sodium alginate. According to the Examiner, the '452 patent discloses a controlled release formulation including polymers of alginic acid such as sodium alginate and hydroxypropylmethylcellulose (HPMC). Further, according to the Examiner, the '871 patent discloses that sustained release polymers include sodium alginate or alginic acid and HPMC, and that they can be formulated into any solid dosage form, such as a gelatin capsule or tablet.

The Examiner states that it would have been obvious to substitute the sustained release polymers and/or tablet form of the '359 publication or '452 and '871 patents for the polymers and/or capsule in the '473 product with predictable results. Further, "[s]uch a substitution of one sustained release polymer of another sustained release polymer is within the purview of the skilled artisan and would yield predictable results." *Id.* at 5. The Examiner further states that adjusting the percent of a compound in the formulation "is simple optimization." *Id.*

Appellant's Position:

1. Claims 1-60 and 66 are non-obvious because no combination of the references teaches the claimed first component comprising sodium alginate, alginic acid, and hypromellose

Claims 1-60 and 66 are non-obvious over the '473 patent, the '359 publication,'452 patent, and the '871 patent because no combination of these references teaches a pharmaceutical formulation having a controlled release component comprising sodium alginate, alginic acid, and hypromellose.

The '473 patent teaches a nitrofurantoin formulation containing the "necessary" sustained release ingredients polyvinylpyrrolidone and carboxyvinylpolymer. See, e.g., '473 patent, col. 6, ll. 35-41; col. 7, ll. 17-20. The '473 patent does not teach alginic acid, sodium alginate, and hypomellose (hydroxypropylmethylcellulose). See, '473 patent, Office Action dated November 9, 2010, p. 5.

The '359 publication is directed to multi-layered pharmaceutical tablets in which hydrophilic polymeric substances in the active layer may comprise HPMC and "alginic acid or a derivative (e.g., sodium or calcium alginate ...)" '359 publication, p. 4, para. 42-43 (emphasis added). The '359 publication teaches that it is preferred that the active layer include both a controlled release polymer, e.g., HPMC, and a viscosity-increasing agent/polymer, e.g., "alginic acid or a derivative (e.g., sodium or calcium alginate ...)." See, '359 publication, p. 3-4, para. 39-43 (emphasis added). The '359 publication does not teach HPMC plus alginic acid and sodium alginate.

The '452 patent discloses a controlled release pharmaceutical formulation comprising "a salt of alginic acid, such as sodium alginate," and a pH independent hydrocarbon gelling agent, such as HPMC. See, e.g., '452 patent, abstract; col. 1, ll. 5-12. There is no teaching in the '452 patent of a pharmaceutical composition comprising alginic acid. According to the '452 patent, alginic acid is only formed after the formulation is acted upon by a patient's gastrointestinal tract following oral administration.

> It is theorized that upon oral ingestion of the sustained release tablet of the invention, in an acid aqueous environment, such as the stomach, the pH independent hydrocolloid gelling agent hydrates to form a gel layer at the surface

> of the tablet. At this low pH environment alginic acid is formed from the alginate salt and this modifies the gel layer around the tablet.

'452 patent, col. 2, ll. 21-28. The instant claims are directed to an orally administrable formulation, such formulations do not include partially digested dosage forms. Thus, the '452 patent does not disclose or suggest the instantly claimed pharmaceutical formulation comprising sodium alginate and alginic acid.

The '871 patent is directed to sustained release pharmaceutical formulations comprising xanthum gum and other optional excipients. See, e.g., '871 patent, abstract. The xanthum gum is responsible for the disclosed sustained release properties and comprises a major portion of the sustained release carrier. See, e.g., '871 patent, col. 2, ll. 16-26. The '871 patent teaches that a "proportion of the xanthum gum" may be replaced by one or more additional polymers having sustained release properties. Examples of such additional polymers according to the '871 patent include "sodium alginate or alginic acid." '871 patent, col. 4, ll. 3-24. The '871 patent discloses the phthalic acid ester of HPMC (i.e., hydroxypropyl methylcellulose phthalate) but not HPMC itself. *Id.* There is no teaching in the '871 patent of a pharmaceutical formulation comprising HPMC, much less a formulation comprising HPMC plus alginic acid and sodium alginate.

For the reasons stated above, no combination of the references teaches an orally administrable formulation comprising nitrofurantoin monohydrate, sodium alginate, alginic acid, and hypromellose. Accordingly, appellants respectfully request that this rejection be withdrawn.

2. Claims 1-60 and 66 are non-obvious because one of ordinary skill in the art would not have replaced "necessary" ingredients in the prior art to arrive at the instantly claimed invention

The instant claims are directed to an orally administrable nitrofurantoin formulation which includes a first controlled release component comprising nitrofurantoin monohydrate, sodium alginate, alginic acid, and hypromellose. The only prior art reference disclosing the instantly claimed active agent, nitrofurantoin, is the '473 patent, which does not disclose the instantly claimed controlled release excipients. The '473 discloses specific sustained release ingredients, and teaches that these ingredients should not be replaced.

The first paragraph of the '473 patent's detailed description states that: "The necessary and optional ingredients are described in detail below." '473 patent, col. 3, ll. 67-68. The next three subheadings describe the necessary ingredients, i.e., "Nitrofurantoin" ('473 patent, col. 4, l. 42), "Polyvinylpyrrolidone" ('473 patent, col. 6, l. 34), and "Carboxyvinylpolymer" (col. 7, l. 16). The fourth subheading is "Optional Ingredients" ('473 patent, col. 8, l. 42). To further emphasize that polyvinylpyrrolidone and carboxyvinylpolymer are irreplaceable ingredients, the '473 patent states that "polyvinylpyrrolidone is a necessary ingredient to achieve sustained release of the nitrofurantoin" ('473 patent, col. 6, ll. 37-39) (emphasis added) and "[c]arboxyvinylpolymer is another necessary ingredient in order to achieve the sustained release pharmaceutical capsules of the present invention" ('473 patent, col. 7, ll. 18-20) (emphasis added). "Necessary" means "absolutely needed : required." http://www.merriam-webster.com/dictionary/necessary (visited September 21, 2010); see Amendment dated September 24, 2010, p. 10.

Upon reading the '473 patent in its entirety (MPEP 2141.02), i.e., taking into account the term "necessary," one of ordinary skill in the art would not have substituted the "necessary" (absolutely needed) controlled release excipients taught in the '473 patent with the instantly claimed controlled release excipients. The '473 patent does not disclose or suggest any permissible interchangeability of the "necessary" controlled release excipients. In view of this teaching, there was no reasonable expectation nor predictability that the "necessary" controlled release excipients of the '473 patent could be substituted successfully.

Further, the '473 patent is the only prior art that is expressly and specifically directed to the instantly claimed active agent nitrofurantoin. One of ordinary skill in the art would not have modified prior art directed specifically to the active agent at issue based on prior art specifying other active agents or active agents generally, particularly when the teaching specific to the instantly claimed active agent requires the ingredients that are subject to the proposed modification.

By stating that certain ingredients are "necessary", the '473 patent expressly teaches that omitting the ingredients, such as by substitution, would render its invention inoperable for its intended purpose. MPEP 2143.01. If this were not the case, the ingredients would not be

"necessary." The Examiner's statement that "[s]imple substitution ... of the sustained release excipients of '473 for other specific sustained release excipients of '359 or '452 and '871 would yield predictable results" may be correct, but not for the reason put forth by the Examiner. The reasonable expectation based upon the prior art teachings is that such a substitution would not work. Appellants' basis for this conclusion is set forth above. The Examiner has not provided support for the bare assertion that one of ordinary skill in the art would reasonably predict a successful outcome, other than that a "skilled artisan would know how" to make such a substitution. Office Action dated November 9, 2010, p. 6, 8, 9. The possibility that a combination can be made is not the standard for obviousness. MPEP 2143.01. The combined prior art does not provide any motivation for replacing the sustained release ingredients taught in the '473 patent. Indeed, the '473 patent teaches away from such substitution because "necessary" ingredients should not be replaced.

In response to appellants' previous arguments (Amendment dated September 24, 2010), the Examiner dismissed the argument that one would not replace "necessary" ingredients, stating that the

> '473 is only relied upon for its teaching of an [sic] sustained release/rapid release oral dosage form comprising a first layer of nitrofurantoin monohydrate and sustained release substituents and a second layer of macrocrystalline nitrofurantoin, and not for its teaching of the instant claimed sustained release excipients ...

Office Action dated November 9, 2010, p. 7-8. A cherry-picking approach such as this is improper. Rather, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." MPEP 21421.02 (citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)). Accordingly, the '473 patent's teaching that polyvinylpyrrolidone and carboxyvinylpolymer are necessary should have been considered.

As stated in (1), above, no combination of the references teaches an orally administrable formulation comprising sodium alginate, alginic acid, and hypromellose. Assuming, for the sake of argument only, that such a combination of ingredients is taught, the only prior art reference directed to the instantly claimed active agent counsels against replacing

its sustained release ingredients with *any* others, including sodium alginate, alginic acid, and hypromellose.

For the reasons stated above, appellants request that this rejection be withdrawn.

3. Claims 17-26, 30, and 37 are non-obvious because no combination of the references teaches the limitations in these dependent claims

The Examiner states that the '473 patent (col. 7, ll. 5-7; col. 8, ll. 29-30) teaches the sustained release polymer weight percents recited in instant claims 17-26, 30, and 37. Office Action dated November 9, 2010, p. 5.

Claims 17-19 recite hypromellose weight percents; claims 20-22 recite sodium alginate weight percents; claims 23-25 recite alginic acid percents; and claims 26, 30, and 37 recite hypromellose, sodium alginate, and alginic acid weight percents. The '473 patent discloses weight percents for polyvinylpyrrolidone (col. 7, ll. 5-7) and carboxyvinylpolymer (col. 8, ll. 29-30). The '473 patent does not disclose the weight percents for the instantly claimed ingredients nor does it teach that the same weight percents may be universally used without regard to the ingredient.

Further, as stated in (1) above, no combination of the prior art teaches, or motivates one of ordinary skill in the art, to include nitrofurantoin, hypromellose, sodium alginate, and alginic acid in an oral formulation. Where the combination of ingredients is not taught, it cannot be routine optimization to determine the amounts of such ingredients. Thus, for this further reason, the rejection of claims 17-26, 30, and 37 should be withdrawn.

4. Claims 50-60 should be allowed because no grounds for rejection have been provided

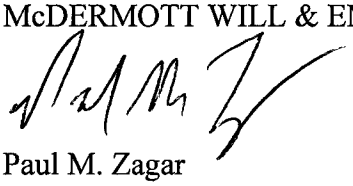
Claims 50-60 are directed to a method for preparing a formulation. Although these claims are listed among the rejected claims, the Examiner has not made out a *prima facie* case of obviousness relating to a method for preparing a formulation. See MPEP 2142 ("[T]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.") (citing *In re Kahn*, 441 F. 3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). Thus, claims 50-60 should not have been included in the rejections. Accordingly, appellants respectfully request that claims 50-60 be allowed.

Conclusion

Based upon the arguments above, Appellants respectfully request that the Honorable Board reverse the Examiner's obvious rejections, and allow claims 1-60 and 66.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



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Claims appendix

1. (Original) An orally administrable formulation for administering nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) said first component comprises nitrofurantoin monohydrate, sodium alginate, alginic acid and hypromellose; (b) said second component comprises macrocrystalline nitrofurantoin; and (c) said formulation provides a therapeutically effective combination of said nitrofurantoin monohydrate and said macrocrystalline nitrofurantoin.

2. (Original) The formulation of claim 1, wherein each of said first and second components independently is in the form selected from the group consisting of granules and powders and wherein said components are provided in a single dosage unit.

3. (Original) The formulation of claim 2, wherein said dosage unit is a tablet.

4. (Original) The formulation of claim 3, wherein said first and second components are present as separate layers.

5. (Original) The formulation of claim 2, wherein said dosage unit is a capsule.

6. (Original) The formulation of claim 1, wherein each of said components is in the form of one or more tablets and said tablets are encapsulated within a single capsule.

7. (Original) The formulation of claim 5, wherein each of said components in said capsule is in the form of granules or powders and said components are present as separate layers.

8. (Original) The formulation of claim 5, wherein one of said components in said capsule is in the form of at least one tablet and the other of said components in said capsule is in the form of granules or powders.

9. (Original) The formulation of claim 1, wherein each of said first and second components is provided as a separate dosage unit.

10. (Original) The formulation of claim 9, wherein each component is provided as at least one tablet.

11. (Original) The formulation of claim 1, wherein said first component comprises from about 25 mg to about 600 mg nitrofurantoin monohydrate.

12. (Original) The formulation of claim 11, wherein said first component comprises from about 50 mg to about 300 mg nitrofurantoin monohydrate.

13. (Original) The formulation of claim 12, wherein said first component comprises from about 75 mg to about 150 mg nitrofurantoin monohydrate.

14. (Original) The formulation of claim 11, wherein said second component comprises from about 5 mg to about 400 mg macrocrystalline nitrofurantoin.

15. (Original) The formulation of claim 14, wherein said second component comprises from about 12 mg to about 200 mg macrocrystalline nitrofurantoin.

16. (Original) The formulation of claim 15, wherein said second component comprises from about 25 mg to about 100 mg macrocrystalline nitrofurantoin.

17. (Original) The formulation of claim 1, wherein from about 5% to about 90% by weight of said first component is hypromellose.

18. (Original) The formulation of claim 17, wherein from about 5% to about 60% by weight of said first component is hypromellose.

19. (Original) The formulation of claim 18, wherein from about 10% to about 30% by weight of said first component is hypromellose.

20. (Original) The formulation of claim 1, wherein from about 2% to about 80% by weight of said first component is sodium alginate.

21. (Original) The formulation of claim 20, wherein from about 5% to about 60% by weight of said first component is sodium alginate.

22. (Original) The formulation of claim 21, wherein from about 10% to about 30% by weight of said first component is sodium alginate.

23. (Original) The formulation of claim 1, wherein from about 2% to about 80% by weight of said first component is alginic acid.

24. (Original) The formulation of claim 23, wherein from about 5% to about 60% by weight of said first component is alginic acid.

25. (Original) The formulation of claim 24, wherein from about 10% to about 30% by weight of said first component is alginic acid.

26. (Original) The formulation of claim 1, wherein said first component comprises nitrofurantoin monohydrate in an amount of about 20% by weight of said first component; hypromellose in an amount of about 20% by weight of said first component; sodium alginate in an amount of about 20% by weight of said first component; and alginic acid in an amount of about 20% by weight of said first component; and said second component comprises macrocrystalline nitrofurantoin in an amount of about 12.5% by weight of said second

component; and said first component and said second component are present in a wt:wt ratio of about 1:1 to about 5:1.

27. (Original) The formulation of claim 1, wherein each of said first and second components further comprises at least one pharmaceutically acceptable carrier, provided that said carrier in said first component does not comprise polyvinylpyrrolidone or carboxyvinylpolymer.

28. (Original) The formulation of claim 27, wherein said carrier comprises a diluent, lubricant, surfactant, glidant or colorant.

29. (Original) The formulation of claim 1 or 26, wherein at least one of said first and second components is coated.

30. (Original) An orally administrable formulation for the administration of nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) said first component comprises: nitrofurantoin monohydrate in an amount of from about 5% to about 50% by weight of said first component; hypromellose in an amount of from about 5% to about 90% by weight of said first component; sodium alginate in an amount of from about 2% to about 80% by weight of said first component; alginic acid in an amount of from about 2% to about 80% by weight of said first component; a diluent in an amount of from about 2% to about 90% by weight of said first component; and a lubricant in an amount of from about 0.1% to about 6% by weight of said first component; and (b) said second component comprises: macrocrystalline nitrofurantoin in an amount of from about 3% to about 35% by weight of said second component; a diluent in an amount of from about 5% to about 90% by weight of said second component; and a lubricant in an amount of from about 0.1% to about 6% by weight of said second component; and said first and second components are present in a wt:wt ratio of from about 1:1 to about 5:1.

31. (Original) The formulation of claim 30, wherein said first or second component further comprises a colorant.

32. (Original) The formulation of claim 31, wherein said colorant is present in an amount of about 0.5% by weight of said second component.

33. (Original) The formulation of claim 30, wherein said first and second components are present in a wt:wt ratio of about 2:1.

34. (Original) The formulation of claim 30, wherein said diluent comprises microcrystalline cellulose, dibasic calcium phosphate, lactose, starch, sucrose or mannitol.

35. (Original) The formulation of claim 30, wherein said lubricant comprises magnesium stearate, talc, calcium oxide, zinc oxide, stearic acid, sodium stearyl fumarate or vegetable oil.

36. (Original) The formulation of claim 30, wherein at least one of said first and second components is coated.

37. (Original) An orally administrable formulation for the administration of nitrofurantoin to a patient in need thereof which comprises: a first component being a controlled release form and a second component being an immediate release form, wherein (a) said first component comprises: nitrofurantoin monohydrate in an amount of about 20% by weight of said first component; hypromellose in an amount of about 20% by weight of said first component; sodium alginate in an amount of about 20% by weight of said first component; and alginic acid in an amount of about 20% by weight of said first component; microcrystalline cellulose in an amount of about 9% by weight of said first component; dibasic calcium phosphate in an amount of about 10% by weight of said first component; and magnesium stearate in an amount of about 1% by weight of said first component; and (b) said second component comprises: macrocrystalline

nitrofurantoin in an amount of about 12.5% by weight of said second component; lactose in an amount of about 43% by weight of said second component; microcrystalline cellulose in an amount of about 43% by weight of said second component; and magnesium stearate with sodium lauryl sulfate in an amount of about 1% by weight of said second component; and said first and second components are present in a wt:wt ratio of from about 1:1 to about 5:1.

38. (Original) The formulation of claim 37, wherein said first or second component further comprises a colorant.

39. (Original) The formulation of claim 38, wherein said colorant is present in an amount of about 0.5% by weight of said second component.

40. (Original) The formulation of claim 37, wherein said first and second components are present in a wt:wt ratio of about 2:1.

41. (Original) The formulation of claim 30 or 37, wherein each of said first and second components independently is in the form selected from the group consisting of granules and powders and wherein said components are provided in a single dosage unit.

42. (Original) The formulation of claim 41, wherein said dosage unit is a tablet.

43. (Original) The formulation of claim 42, wherein said first and second components are present as separate layers.

44. (Original) The formulation of claim 37, wherein said dosage unit is a capsule.

45. (Original) The formulation of claim 37, wherein each of said components is in the form of one or more tablets and said tablets are encapsulated within a single capsule.

46. (Original) The formulation of claim 44, wherein each of said components in said capsule is in the form of granules or powders and said components are present as separate layers.

47. (Original) The formulation of claim 44, wherein one of said components in said capsule is in the form of at least one tablet and the other of said components in said capsule is in the form of granules or powders.

48. (Original) The formulation of claim 30 or 37, wherein each of said first and second components is provided as a separate dosage unit.

49. (Original) The formulation of claim 48, wherein each component is provided as at least one tablet.

50. (Original) A method for preparing a formulation which comprises (a) admixing nitrofurantoin monohydrate, hypromellose, alginic acid sodium alginate and at least one pharmaceutically acceptable carrier and forming said admixture into a controlled release first component; and (b) admixing macrocrystalline nitrofurantoin and at least one pharmaceutically acceptable carrier and forming said admixture to form an immediate release second component.

51. (Original) The method of claim 50, further comprising encapsulating said first and second components.

52. (Original) The method of claim 50, wherein each of said first and second components independently is in the form selected from the group consisting of granules and powders and wherein said components are formed into a single dosage unit.

53. (Original) The method of claim 50, wherein said dosage unit is a tablet.

54. (Original) The method of claim 53, wherein said first and second components are present as separate layers.

55. (Original) The method of claim 52, wherein said dosage unit is a capsule.

56. (Original) The method of claim 50, wherein each of said components is in the form of one or more tablets and said tablets are encapsulated within a single capsule.

57. (Original) The method of claim 55, wherein each of said components in said capsule is in the form of granules or powders and said components are present as separate layers.

58. (Original) The method of claim 55, wherein one of said components in said capsule is in the form of at least one tablet and the other of said components in said capsule is in the form of granules or powders.

59. (Original) The method of claim 50, wherein each of said first and second components is formed into a separate dosage unit.

60. (Original) The method of claim 59, wherein each component is provided as at least one tablet.

61. (Withdrawn) A method for treating a bacterial infection in a host which comprises administering to said host said formulation of claim 1, 30 or 37.

62. (Withdrawn) The method of claim 61, wherein said first component and said second component of said formulation are present in a wt:wt ratio of about 2:1 to about 3:1.

63. (Withdrawn) The method of claim 62, wherein said first component and said second component are present in a wt:wt ratio of about 2:1.

64. (Withdrawn) The method of claim 61, wherein nitrofurantoin monohydrate and macrocryststalline nitrofurantoin are present in a combined weight of about 100 mg.

65. (Withdrawn) The method of claim 64, wherein said formulation is administered two times per day for a period of about 7 days.

66. (Original) The formulation of claim 37, wherein at least one of said first and second components is coated.

Evidence appendix

None

Related proceedings appendix

None